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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SUGHRUE MION ZINN MACPEAK & SEAS PLLC
2100 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 200373213

EXAMINER
EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/429,003	SHARMA ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2001 and 05 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10, 19* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is written in response applicant's correspondences submitted 8/13/01, paper number 16 and 11/5/01, paper number 20. Claims 18-30 have been cancelled and claims 37-65 were added. Claims 37-65 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

2. The information disclosure statement filed 11/5/01 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because several of the non-patent references were not received, and one of the references is improperly cited. The references not received are those written by Lonneborg *et al.*, Fujioka, Schena (the Bioessays citation), and Shalon *et al.* Furthermore, the Zhi-Xin *et al.* references is not properly cited on the 1994 because no journal is listed for this reference. The 1449 has been placed in the application file, but the citations that are not initialed have not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

3. The IDS filed 9/28/2000 has been considered. An initialed copy of the 1449 is being mailed with this office action.

Claim Objections

4. Claims 60-65 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiply depending claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 37-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "and originate from" in claims 37-65 appears to represent new matter. Applicant indicated in paper number 16 that support for the amendments (which included the "and originate from" language) can be found at page 23 lines 15 *et seq*. Applicant indicated in paper number 20 that support for the instant amendments can be found in the claims as originally filed and at page 7, lines 30-35. However, these sections of the specification do not provide basis for the limitation which requires that the cells whose mRNA is being isolated originate distant from the site of disease. At page 23, the specification

discusses that samples may "originate from different parts of the body." At page 7, the specification provides definitions for the use of the words tissue, cells, and body fluids. The specification does not, however, specify that the cells contained within the samples originate from distant parts of the body. For example, blood contains an amalgamation of cells, which may originate from many different parts of the body. Thus, in the case of a prostate cancer, a blood sample would originate from a part of the body distant from the cite of the disease. That blood sample may contain cells from all over the body. The specification, in neither the description nor the examples, never specifically provides basis for a limitation which requires that the mRNA tested comes from cells which originate from a site distant from the disease. The mere statement that the sample may originate from a distant part of the body does not distinguish where the cells themselves in the sample originate. Since no basis has been identified, the claims are rejected as incorporating new matter.

7. Claim 36-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of obtaining isolated selected mRNA species useful for diagnosing or identifying a disease or condition wherein the mRNA is isolated from cells that are obtained a part of an organism distant to the area of disease, does not reasonably provide enablement for methods of obtaining isolated selected mRNA species useful for diagnosing or identifying a disease or condition wherein the mRNA is isolated from cells that are obtained from and originate from a part of an organism distant to the area of disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to methods of obtaining isolated selected mRNA species "useful for diagnosing or identifying a disease or condition." The claims are also drawn to gene probe diagnostic kits which contain probes identified by the methods for obtaining isolated selected mRNA species, as well as methods for diagnosing patients using said the products identified by the methods for obtaining isolated selected mRNA species. Some of the claims recite that the probes will be useful for diagnosing specific diseases such as Alzheimers disease and cancer (stomach, lung, breast, prostate, bowel, and skin). The claims specifically recite the isolation of mRNA from cells of organisms that have a disease and the isolation of mRNA from healthy organisms. The cells are required to be "obtained from, and originate from a part of said organism distant to the area of said disease."

The specification does not provide a single working example wherein the instantly claimed method was used to obtain isolated selected mRNA species useful for diagnosing or identifying a disease or condition, and the specification specifically does not provide a single working example in which the method was used to obtain isolated selected mRNA species useful for diagnosing or identifying a disease such as Alzheimer's disease or cancer. The examples provided in the specification are largely prophetic, and do not provide clear data which indicates the functionality of this invention. Examples 1 and 2 provide direction as to the use of this invention for the diagnosis of Alzheimer's disease and senile dementia, however, they do not provide the transcript patterns necessary or any specific probes useful for the diagnosis. Example 4 appears to provide the use of a differential expression methodology for the production of a diagnostic transcript pattern for Arabidopsis, however, the specification does not provide any data as to the disease being studied. Thus, it is unclear if the disease is systemic or localized.

It is not clear if the tissue samples taken were from the location of the disease or from some other disease. The example states that it is leaves that are sampled, but it gives no indication if it was healthy leaves or diseased leaves. Example 5 provides a prophetic example of humans, merely stating that results would be expected to be "similar to those in figure 1." The result in figure 1 appear to be hypothetical results. Finally, in example 6, a differential expression type methodology is used to analyze infection for a fungal pathogen in Norway spruce. The example does not make clear if the roots and upper parts whose mRNA is isolated is itself is isolated from cells obtained from a location "distant" from the infection, let alone that the cells whose mRNA are isolated themselves are distant from an infection.

The prior art provides extensive guidance as to the use of differential expression methodology for the identification of probes useful for the detection of disease (see, for example, Graber *et al.* or Ditkoff *et al.*, cited in previous actions). With regard to the identification of nucleic acid probes which are isolated from cells that originate from a location distant from the point of disease, the prior art provides only two examples. Ralph *et al.* (US 6190857) provide probes which identify genes that are expressed in the peripheral blood of individuals with prostate or breast cancer compared to normal individuals. Zhi-Xin *et al.* (Zhongguo Zhongliu Linchuang (1996) Vol. 23, No. 4, pp. 243-246) teach that IL-2R expression in peripherial blood mononuclear cells is closely associated with the presence of tumor metastasis in lung cancer patients. These teachings in the art, therefore, enable the instant method for use in prostate, breast, and lung cancer. In addition, the prior art provides disclosure of arrays which contain over a thousand different cDNAs derived from human blood.

The prior art does not provide any guidance with regard to the identification of nucleic acid probes which are isolated from cells that originate from a location distant from the point of disease for diseases in other types of cancers or other types of diseases. The diagnosis of Alzheimer's disease is quite difficult, and the confirmation of such a diagnosis is currently only possible post-mortem.

While level of skill in the art (i.e. a PhD in biochemistry) is quite high, but the unpredictability associated with identifying isolated selected mRNA species which are obtained from cells which originate from a location distant from the point of disease and are useful for the detection of diseases is higher. The human blood, for example, expresses hundreds of thousands of different transcripts, and which of these particular transcripts would be useful for the detection of any particular disease is highly unpredictable. The determination of such an association requires extensive laboratory work, as is exemplified by the teachings of Ralph *et al.* In order to enable the instant claims to their current breadth, some showing that the method functions for a representative number of diseases would be required. Since the claims embrace diagnostics for any disease or condition in any eukaryote, a representative number would have to include different eukaryotes and a variety of diseases. No such showing is provided in the instant specification.

Furthermore, it is noted that the product claims 53-55 and the methods for diagnosis (claim 59) all depend on the specific use of the probes identified by the methods of claims 37-52. Thus, for all of the reasons discussed above, these claims are also not enabled.

Because of the lack of working examples, the high level of unpredictability in the art, the lack of guidance provided in the specification or the art, and the high level of experimentation

necessary to practice the claimed invention, it is concluded that undue experimentation would be necessary to practice the claimed invention.

8. Claims 53-55, and 59-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to gene transcript pattern probe kits and method for using such kits in the diagnosis of disease. The claims depend from base claims which describe methods for isolating the probes in question. However, as discussed above, the specification does not enable the methods from which these claims depend. Furthermore, the instantly rejected claims do nor provide any structure as to what probes are contained in the instantly claimed and used probe set. Essentially, these claims are drawn to probes whose actual sequences are completely unknown. Thus, the large genus is represented in the specification by no species in a genus which comprises hundreds of millions of different possibilities.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only a method for obtaining the claimed nucleic acid sequence is described. No guidance is given as to the structure of the claimed probe sets. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acid sets or methods for using the nucleic acid sets as instantly claimed.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 37, 40, 41, 42, 45, 46, 48, 49, 50, and 51 are rejected under 35 U.S.C. 102(e) as being anticipated by Ralph *et al.* (US 6190857).

Ralph *et al.* teach a method of obtaining isolated selected cDNA species useful for diagnosing or identifying a disease or condition (prostate or breast cancer) or a stage thereof in a eukaryotic organism comprising the steps of:

(a) isolating mRNA from cells of one or more eukaryotic organisms (humans) which are known to have said disease or condition or a stage thereof, wherein said cells are obtained from, and originate from, a part of said organism distant to the area of said disease (blood), wherein the

resulting isolated mRNA is subjected to reverse transcription and amplification to obtain isolated cDNA (Col. 62, lines 33-60);

(b) isolating mRNA from corresponding cells of one or more corresponding normal eukaryotic organisms wherein the resulting isolated mRNA is subjected to reverse transcription and amplification to obtain isolated cDNA (Col. 62, lines 33-60);

(c) separating via gel electrophoresis and an ethidium bromide label, a non-sequence based separation technique, cDNA species present within each of the resulting isolated cDNA of step (a) and (b) (Col. 62, lines 63-64);

(d) selecting two or more cDNA species from the resulting separated cDNA species obtained in step (c), which are present at a different level in the normal sample than in the diseased sample by identifying a signal corresponding to each cDNA species (Col. 62, line 64);

(e) isolating the resulting two or more selected cDNA species obtained in step (d) (Col. 62, line 65).

Claim Rejections - 35 USC § 103

11. Claims 37-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wadhwa *et al.* (Molecular Biotechnology, Vol. 6, 1996, p. 213-217) in view of Zhi-Xin *et al.* (Zhongguo Zhongliu Linchuang (1996) Vol. 23, No. 4, pp. 243-246).

Wadhwa *et al.* teach a method of obtaining isolated selected cDNA species which comprising:

(a) isolating mRNA from a normal mouse cell line, reverse transcribing the mRNA, amplifying the cDNA, and labeling the resulting cDNA with denaturing loading dye (p. 214);

(b) isolating mRNA from a transformed clone, reverse transcribing the mRNA, amplifying the cDNA, and labeling the resulting cDNA with denaturing loading dye (p. 214);

(c) separating the cDNA species using gel electrophoresis (p. 214)

(d) selecting two or more cDNA species from the separated cDNA species obtained in step (c), which are present at a different level in the normal sample than in the diseased sample (Fig. 1)

(e) isolating and amplifying the resulting selected cDNA species (p. 215); and

(f) immobilizing the resulting isolated selected cDNA species on a Hybond N^+ membrane filter (p. 215).

Wadhwa *et al.* further teach that 16 primer pairs were used to amplify the cDNA's, and that for each of these primer pairs 3-5 differentially expressed bands were seen in either of the two samples (p. 215), resulting in a total of 48-80 differentially expressed bands, and that all of theses bands were isolated from the gel (p. 215).

Wadhwa *et al.* do not teach the use of such a method for obtaining diagnostic probes, nor do the teach methods for diagnosis as instantly claimed. However, Wadhwa *et al.* make it clear that their methods are for improving differential display methodology which is a "simple, sensitive, and powerful method to identify differentially expressed genes in in vitro and in vivo biological systems from different origins or under different biological conditions. Wadhwa *et al.* do not teach methods wherein the cells are obtained from, and originate from, are taken from a part of the organism distant to the area of said disease.

Zhi-Xin *et al.* that IL-2a mRNA expression in peripheral blood mononuclear cells of patients with lung cancer when compared to a control group, and that IL-2R expression level was

closely related to prognosis in cancer patients (pages 243-246). Thus, Zhi-Xin provide an example of differential expression that are diagnostic of cancer in cells that are obtained from, and originate from a site distant from the tumor.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the methods for obtaining isolated selected mRNA species useful for diagnosing or identifying a disease as taught by Wadhwa *et al.* by sampling cells which are obtained from, and originate distant from the site of disease, such as blood cells, as taught by Zhi-Xin *et al.* in order to identify additional mRNA species useful for disease detection. The ordinary practitioner would have been motivated to combine these methods because Wadhwa *et al.* teach that "Differential display of mRNA species has recently been developed as a simple, sensitive, and powerful method to identify differentially expressed genes in in vitro and in vivo biological systems from different origins or under different conditions (p. 213)" and Wadhwa *et al.* exemplify that in fact the expression of certain mRNA species in cells which are obtained from and originate from an area distant from disease has important diagnostic value. The ordinary practitioner would have been motivated to combine these methods to provide a method for determining additional sequences with diagnostic utility.

12. Claims 37, 40-42, 45, 46, 48, 49, 50, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graber *et al.* (Annals of Surgical Oncology, 3(2): 192-197) in view of Zhi-Xin *et al.* (Zhongguo Zhongliu Linchuang (1996) Vol. 23, No. 4, pp. 243-246).

Graber *et al.* teach a method of obtaining isolated selected cDNA species which comprising:

(a) isolating mRNA from a normal esophageal mucosa tissue sample, reverse transcribing the mRNA, and amplifying the cDNA (p. 193);

(b) isolating mRNA from a carcinoma of the esophagus sample, reverse transcribing the mRNA, and amplifying the cDNA (p. 193);

(c) separating the cDNA species using gel electrophoresis (p. 193)

(d) selecting two or more cDNA species from the separated cDNA species obtained in step (c), which are present at a different level in the normal sample than in the diseased sample (Fig. 1); and

(e) isolating the resulting selected cDNA species by excision from the gel (p. 194).

The tissue samples were human tissue obtained from The Cooperative Human Tissue Network of the National Disease Research Institute or from patients. With regard to claim 23, which requires that the cDNA is labeled, Graber *et al.* do not expressly teach this limitation, however, labeling of the cDNA is an inherent property of the autoradiography method that Graber *et al.* use to visualize the bands (p. 193, Fig. 1).

Graber *et al.* do not teach the use of such a method wherein the cells whose mRNA is isolated from cells that are obtained from, and originate from a part of the organism distant to the area of said disease.

Zhi-Xin *et al.* that IL-2a mRNA expression in peripheral blood mononuclear cells of patients with lung cancer when compared to a control group, and that IL-2R expression level was closely related to prognosis in cancer patients. Thus, Zhi-Xin provide an example of differential expression that are diagnostic of cancer in cells that are obtained from, and originate from a site distant from the tumor.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the methods for obtaining isolated selected mRNA species useful for diagnosing or identifying a disease as taught by Graber *et al.* by sampling cells which are obtained from and originate from parts of the body distant from the site of disease, such as blood cells, as taught by Zhi-Xin *et al.* in order to identify mRNA species useful for disease detection. The ordinary practitioner would have been motivated to combine these methods because Graber *et al.* teach that "differential display can be used to isolate cDNAs of widely varying levels of expression (p. 196)," and they further teach that genes can be identified "without any prior knowledge of their sequence or function (p. 193), and Zhi-Xin *et al.* exemplify that in fact the expression of certain mRNA species at an area distant from disease has important diagnostic value. The ordinary practitioner would have been motivated to combine these methods to provide a method for determining additional sequences with diagnostic utility.

13. Claims 53-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wadhwa *et al.* in view Zhi-Xin *et al.* as applied to claims 37-51 above, and further in view of the Stratagene Catalog (1988).

The teachings of Wadhwa *et al.* in view of Zhi-Xin *et al.* are applied herein as discussed above. It is especially noted that Wadhwa *et al.* teach methods in which labeled cDNA samples (both normal and transformed samples) are exposed to the immobilized cDNA species to produce a gene transcript pattern.

Wadhwa *et al.* in view of Zhi-Xin *et al.* do not teach the packaging of the immobilized cDNA species into a kit, nor do they teach this method as a method for making a kit.

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to use the method disclosed by Wadhwa *et al.* in view of Zhi-Xin *et al.* to produce a kit containing the cDNAs on a solid support and other reagents useful for gene transcript comparisons, such as the a normal and diseased samples as taught by Wadhwa *et al.* in view of Zhi-Xin *et al.* to be used in nucleic acid research since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

It is noted that these claims contain a preamble which recites an intended use, however, it is also noted that this use does not confer patentable weight on the product claims since the preamble does not materially change what is present in the kit itself and thus represents an intended use of the kit (see MPEP 2111.02). Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Wadhwa *et al.* in view of Zhi-Xin *et al.*, further in view of the Stratagene catalog.

14. Claims 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wadhwa *et al.* in view of Zhi-Xin *et al.* in view of the Stratagene Catalog as applied to claims 53-58 above, and further in view of Seilhamer *et al.* (WO 95/20681).

The teachings of Wadhwa *et al.* in view of Zhi-Xin *et al.* in view of the Stratagene Catalog is applied to this claim as discussed above.

Wadhwa *et al.* in view Zhi-Xin *et al.* in view of the Stratagene Catalog do not teach a method in which a test sample is compared to a known sample for diagnosis of a disease.

Seilhamer *et al.* teach that a gene transcripts from a biological specimen can be quantified and compared to against the transcripts of a diseased and healthy patients in order to diagnose a disease (p. 12, lines 5-20). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included such a comparison step in the methods taught by Wadhwa *et al.* in view of Zhi-Xin *et al.* in view of the Stratagene catalog in order to have provided a method for the diagnosis of disease since Seilhamer teach that such comparisons are useful for disease diagnosis.

15. Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schena *et al.* (PNAS USA, Vol. 93, pp. 10614-10619) in view of the Stratagene Catalog.

Schena *et al.* teach a microarray containing 1046 human cDNAs isolated from human peripheral blood lymphocytes (p. 10614). The genes immobilized thereon would comprise two or more mRNA species that are useful for diagnosing a disease or condition. It is noted that the instant claims are broadly drawn to require only that the solid support "have" on it mRNA or cDNA species that were isolated by the methods of the recited claims. The language "having" is open claim language interpreted to be equivalent to "comprising." It is noted that product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps (see MPEP 2113). Thus, the microarray taught by Schena *et al.* would inherently be a solid support having a probe useful for the diagnosis of disease.

Schena *et al.* do not teach the packaging of this microarray into a kit.

Stratage teaches gene characterization kits. The ordinary practitioner would have been motivated to produce a kit containing the microarray taught by Schena *et al.* and other reagents useful for gene transcript comparisons, to be used in nucleic acid research since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

It is noted that these claims contain a preamble which recites an intended use, however, it is also noted that this use does not confer patentable weight on the product claims since the preamble does not materially change what is present in the kit itself and thus represents an intended use of the kit (see MPEP 2111.02). Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Schena *et al.* in view of the Stratagene catalog.

RESPONSE TO REMARKS

Applicant's arguments focus on the fact that the previous rejections did not address the limitation in the claim that the cells originate from a location distant from the point of disease. These rejections have been withdrawn and new grounds of rejection have been set forth herein. The new grounds of rejection thoroughly address the newly added claims, and therefore the arguments put forth in paper number 16 are moot. Paper number 20 does not set forth any additional arguments.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1655

January 24, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600